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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,267	08/20/2003	Heather Lynn Davis	C1040.70012US00	6263

7590 10/16/2008

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EXAMINER	
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ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
10/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/644,267	DAVIS ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-53* is/are pending in the application.

4a) Of the above claim(s) *48-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/146,072.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/22/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed July 22, 2008 (hereinafter referred to as "the response") has been entered. No amendments have been made.

The elected invention is drawn to a method of inducing an antigen specific immune response in a subject by administration of an expression plasmid encoding a hepatitis B virus (HBV) antigen.

Claims 32-53 are pending in the instant application.

Claims 48-53 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention. Election was made **without** traverse in the reply filed on July 27, 2006.

Accordingly, Claims 32-47 are examined herein.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 22, 2008 has been entered.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d

887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 32-47 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-14 of U.S. Patent No. 6,635,624. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the earlier-filed application are directed to a species that falls within the presently claimed genus. Thus, the claims of the patent anticipate the present claims (anticipation analysis).

At page 5 of the response, Applicants state that they may file a terminal disclaimer depending on the claims that are found to be allowable.

Accordingly, the rejection is maintained for reasons of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32-47 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method as claimed, wherein the vector comprises a gene encoding the hepatitis B

virus surface antigen protein, and further wherein the vector comprises a promoter operably linked to the gene, such that the antigen is expressed in a mammal, does not reasonably provide enablement for the use of a vector encoding any other HBV antigen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to a method of inducing an antigen specific immune response in a subject by administration of an expression plasmid encoding a hepatitis B virus (HBV) antigen.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, are set forth in *In re Wands*, 8 USPQ2d 1400, at 1404 (CAFC 1988). These factors include: (1) the nature of the invention, (2) the state of the prior art, (3) the relative level of skill of those in the art, (4) the predictability of the art, (5) the breadth of the claims, (6) the amount of direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary.

Enablement has been evaluated giving due consideration to all the Wands factors, and the following factors are particularly noteworthy:

The state of the art of DNA vaccination is such that there are several significant limitations to the application of the same methodology in different species. Studies looking at the efficacy of DNA immunization using similar approaches in humans or large animals are "not encouraging" since DNA vaccines are "often less effective in large animals than in mice" (Babiuk et al., 2003).

In an article published well after the filing date of the instant application, Rubanyi (2001) teaches that the problems described above remain unsolved at the time the instant application was filed. Rubanyi states, "[a]lthough the theoretical advantages of [human gene therapy] are undisputable, so far [human gene therapy] has not delivered the promised results: convincing clinical efficacy could not be demonstrated yet in most of the trials conducted so far …" (page 113, paragraph 1). Among the technical hurdles that

Rubanyi teaches remain to be overcome are problems with gene expression control systems (see especially the section under "3. Technical hurdles to be overcome in the future", pages 116-125).

Beyond the technical barriers to all gene therapy approaches, each disease to be treated using gene therapy presents a unique set of challenges that must be addressed individually. The claimed methods encompass the use of a wide variety of genetic constructs to treat a wide variety of diseases. Rubanyi teaches, "each disease indication has its specific technical hurdles to overcome before gene therapy can become successful in the clinic (p. 131, paragraph 4). Rubanyi states, "the most promising areas for gene therapy today are hemophilias, for monogenic diseases, and cardiovascular disease (more specifically, therapeutic angiogenesis for myocardial ischemia and peripheral vascular disease…) among multigenic diseases" (p. 113, paragraph 4). As of the filing date of the instant application however, even the most promising areas presented barriers to successful gene therapy that could not be overcome by routine experimentation. Rather, the prior art shows that intensive investigation has met with limited success.

The court has recognized that physiological activity is unpredictable. *In re Fisher*, 166 USPQ 18 (CCPA 1970). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved. *In re Fisher*, 166 USPQ 18 (CCPA 1970).

It is not to be left up to the skilled artisan to figure out how to make the necessary starting materials and then to figure out how to use them to produce the biological effects as recited in the claims. The courts held that the disclosure of an application shall inform those skilled in the art how to use applicant's claimed invention, not how to **find out** how to use it for themselves. *In re Gardner et al.* 166 USPQ 138 (CCPA 1970). This specification only teaches what is intended to be done and how it is intended to work, but does not actually teach how to do that which is intended.

Given the unpredictability in the DNA vaccination and gene therapy art, and further given that the specification fails to provide specific guidance on which antigens (and genes encoding them) can be used to produce a protective immune response, across the very broad scope, the skilled artisan would have been required to engage in undue experimentation to develop a method within the scope of the claims for using any HBV antigen-encoding gene other than a gene encoding a surface antigen.

At page 6 of the response, Applicants assert that their analysis supports a scope of enablement of the HBV antigen genus as claimed. Applicants note that the breadth of the genus of hepatitis B virus antigens is at issue and that exemplary HBV antigens are disclosed in the specification and include HBV proteins and portions of proteins (i.e., fragments) such as HBV surface antigens and core antigens. Applicants further note that other HBV antigens were known in the art at the time of the invention, including HBV e-antigen, DNA polymerase, and x-antigen. Applicants also assert that HBV core antigens were known to induce specific immune responses in chimpanzees and to protect the animals against HBV during challenge experiments. Applicants further allege, citing U.S. Patent No. 5,019,386 (Machida et al.), that HBV antigenic peptides that induce specific immune responses were also known at the time of the invention. However, protein/peptide vaccination is not DNA vaccination and the results obtained through protein vaccination do not reasonably correlate to the results obtained with DNA vaccination. As noted in the rejection of record, the issue is getting sufficient expression of an antigen in the appropriate location to raise a protective immune response. Numerous parameters affect delivery of the DNA and intracellular trafficking of the expressed protein. In 1993, the effective filing date of the instant application, methods of DNA vaccination were in their infancy and little was known about the consequences of different routes of delivery and the biological effects of different DNA delivery techniques. References teaching protein vaccination do not resolve the technical hurdles pertaining to DNA vaccination techniques.

At page 7, paragraph 1 of the response, Applicants allege that the nature of the invention is a method of inducing a specific immune response to an HBV antigen, and that specific immune responses include humoral responses and cell-mediated responses. However, Applicants fail to acknowledge that the nature of the invention lies in the DNA vaccination technique used to raise the antigen-specific immune response. Accordingly, Applicants do not address the barriers inherent to DNA vaccination approaches.

At page 7, paragraph 2 of the response, Applicants assert that the state of the prior art at the time of the invention was such that HBV antigens capable of inducing specific immune responses were well known and that methods for detecting, cloning, and sequencing HBV genomic DNA were routine and available to the skilled artisan. However, it is not sufficient to obtain genes encoding HBV antigens, as the issue is which genes to use and how to deliver and express the genes so that a protective immune response is raised. Cloning various genes of the HBV genome does not address these issues.

At page 7, paragraph 3 of the response, with regard to the level of predictability in the art, Applicants reiterate that it is the scope of the HBV antigen genus that is in question, and not the method for inducing an antigen specific immune response per se. Applicants are mistaken because it is the DNA vaccination approach for the broad scope of any HBV antigen other than a surface antigen that is at issue. As noted in the rejection of record, the technical hurdles that remain to be overcome are problems with gene expression control systems, the mode of DNA delivery, and efficient expression in mammalian species other than mice. Applicants further allege that a gene encoding an HBV antigen can be cloned into an expression vector and expressed in a subject to produce an antigen specific immune response. However, the art cited in the rejection of record amply demonstrates that DNA vaccination approaches are not analogous to protein vaccination approaches and that adequate levels of antigen expression for raising a protective immune response are often not achieved with DNA vaccination. As noted above, in 1993, methods of DNA vaccination were in their infancy and little was known about the consequences of

different routes of delivery and the biological effects of different DNA delivery techniques. In 2003, ten years after the effective filing date of the instant application, Babiuk et al. (2003) showed that gene gun delivery and the induction of mucosal immunity were superior to other modes of delivery of plasmid DNA for immunization of large animals and **necessary** for producing a protective effect. Absent the enhanced expression, protective effects were not seen.

At page 7, paragraph 4 of the response, Applicants assert that the level of skill in the art was such that a person of ordinary skill would have been able to identify an appropriate HBV antigen and prepare an expression plasmid vector capable of expressing the antigen in a subject. Applicants further assert that the skilled artisan would have been capable of administering the expression plasmid vector according to the claimed method to induce an antigen specific immune response in a subject. However, as noted in the rejection of record, the technical hurdles that remain to be overcome are problems with gene expression control systems, the mode of DNA delivery, and efficient expression in mammalian species other than mice, for antigens other than HBV surface antigens. Therefore, preparation and administration of an expression plasmid is not sufficient to provide for appropriate delivery of the gene, sufficient levels of expression of the gene, and proper presentation of the antigen to the immune system, such that a protective immune response is raised.

At page 8 of the response, Applicants assert that the specification provides working examples that demonstrate induction of specific immune responses to HBV antigens. However, while the working examples adequately teach how to raise a protective immune response when surface antigen genes are administered by a DNA vaccination approach, the specification does not teach how to achieve the same effect using non-surface antigen genes. Further, given the unpredictability in the art, the skilled artisan would not be able to achieve such an effect with other genes, absent undue experimentation.

At page 8 of the response, Applicants conclude that the amount of experimentation needed for one of ordinary skill in the art to carry out the claimed methods is reasonable. Applicants allege that, to

carry out the methods with a non-surface antigen, the skilled artisan need only select a HBV non-surface antigen as disclosed in the specification or known in the art, obtain or prepare and expression plasmid vector encoding the antigen, and carry out the administration method in a subject. This argument has already been addressed above. Preparation and administration of an expression plasmid is not sufficient to provide for appropriate delivery of the gene, sufficient levels of expression of the gene, and proper presentation of the antigen to the immune system, such that a protective immune response is raised. The type of immune response raised depends on the particular antigen gene used, its expression control sequences, the mode of DNA delivery, and the intracellular trafficking of antigen once expressed.

At page 9 of the response, Applicants assert that a considerable amount of experimentation is permissible for enablement and that Babiuk et al. (2003) discusses several approaches for improving the efficiency of a DNA vaccine, but does not suggest that such vaccines are unpredictable. Applicants conclude that Babiuk supports predictability in the art of DNA vaccines. On the contrary, the studies reported by Babiuk et al. showed that gene gun delivery and the induction of mucosal immunity were superior to other modes of delivery of plasmid DNA for immunization of large animals and **necessary** for producing a protective effect. Absent the enhanced expression, protective effects were **not seen**. In contrast, in 1993, methods of DNA vaccination were in their infancy and little was known about the consequences of different routes of delivery and the biological effects of different DNA delivery techniques. Furthermore, for the reasons detailed below, the instant specification does not enable gene gun delivery of plasmids encoding antigens and the teachings of Babiuk et al. are specific to gene gun delivery. Babiuk et al. (2003) is post-filing art and therefore one of skill in the art would not have had the benefits of its teachings at the time of the invention. In 1993, there were no clear guidelines for improving the *in vivo* expression of an antigen from a plasmid vector to achieve expression levels sufficient to produce a protective effect in large animals. Given the problems acknowledged by those skilled in the art, this is the epitome of unpredictability. The unpredictability of a particular art area may

alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See *Ex parte Singh*, 17 USPQ2d 1714 (BPAI 1991). It is also well established in case law that the specification must teach those of skill in the art how to make and how to use the invention as broadly claimed. *In re Goodman,* 29 USPQ2d at 2013 (Fed. Cir. 1994), citing *In re Vaeck*, 20 USPQ2d at 1445 (Fed. Cir. 1991).

At page 9 of the response, Applicants assert that Rubanyi is a chapter on gene therapy and deals with the factors essential for clinical efficacy and safety. Applicants allege that the discussion of technical hurdles is within this context of clinical efficacy and safety and therefore Applicants dismiss the teachings of Rubanyi as not relevant to determining the scope of enablement of the claimed invention. However, Rubanyi is cited for its teachings regarding technical hurdles hindering *in vivo* gene expression, not for issues of safety. Among the technical hurdles that Rubanyi teaches remain to be overcome are problems with gene expression control systems (see especially the section under "3. Technical hurdles to be overcome in the future", pages 116-125). The field of gene therapy broadly includes any method that involves *in vivo* expression of an exogenously administered nucleic acid vector for production of a therapeutic effect, and is not limited to gene replacement techniques. Accordingly, the field of gene therapy is the appropriate field of inquiry concerning *in vivo* expression of exogenous DNA constructs.

At page 10, paragraph 1 of the response, Applicants cite Yang et al. (2006) for showing that DNA vaccination in human subjects results in T cell activation that is specific for HBV antigens, both envelope and core antigens. However, the cited reference is post-filing art and describes a vaccination protocol that is distinct from what is taught in the instant specification. Multiple plasmids encoding multiple antigens were used in combination with a genetically engineered interleukin-12 DNA in patients receiving chemotherapy (lamivudine). Thus, the DNA vaccination protocol was not carried out in accordance with the teachings of the instant specification, and given that the reference is post-filing art, one of skill in the art would not have had the benefits of its teachings at the time of the invention.

At page 10, paragraph 2 of the response, Applicants assert that Tabor (USPN 4,547,367) teaches that HBV core antigens induce a protective immune response in non-human primates. Applicants further assert that the administration of an expression plasmid vector that expresses a HBV core antigen according to the claimed methods is expected to induce a protective and specific immune response in multiple species including primates. No support is offered for this assertion. Protein/peptide vaccination is not DNA vaccination and the results obtained through protein vaccination do not reasonably correlate to the results obtained with DNA vaccination. As noted in the rejection of record, the issue is getting sufficient expression of an antigen in the appropriate location to raise a protective immune response. Numerous parameters affect delivery of the DNA and intracellular trafficking of the expressed protein. In 1993, the effective filing date of the instant application, methods of DNA vaccination were in their infancy and little was known about the consequences of different routes of delivery and the biological effects of different DNA delivery techniques. References teaching protein vaccination do not resolve the technical hurdles pertaining to DNA vaccination techniques.

At page 10, paragraph 3 of the response, Applicants assert that the Examiner has mischaracterized the reference of Haynes et al. (1996). Applicants assert that the cited section notes that several reports demonstrate that DNA vaccination elicits humoral, protective, and cytotoxic cellular immune responses. However, the reference does **not** describe the use of DNA immunization to elicit cytotoxic T cell responses to hepatitis B. With regard to hepatitis B, the reference teaches only the induction of antibody responses in DNA vaccination experiments. The results presented therein are specific to particle-mediated genetic immunization. In fact, the authors explicitly state that "[t]he observation that immunological results similar to those seen in rodents can also be achieved in larger animals is likely due to the physical nature of this delivery process" (page 41, column 1, paragraph 2). The instant specification does not describe or discuss particle-mediated methods of DNA vaccination at all. There is no mention or contemplation of the use of particle-mediated methods of DNA vaccination in the instant

specification. The instant specification is directed exclusively to intramuscular administration of a plasmid vector encoding an HBV antigen. With regard to the genetic immunization of rhesus monkeys using a vector encoding the hepatitis B core antigen (HBcAg) driven by the CMV promoter, the results reported are specific to particle-mediated (gene gun) delivery of DNA to the skin. Furthermore, although HBcAg-specific antibody titers are reported, there is no evidence that the antibody response provided a protective effect. Given that the reference of Haynes et al. (1996) is post-filing art, the skilled artisan would not have had the benefits of its teachings of with regard to gene gun-mediated immunization of the skin at the time of the instant invention. Thus, it cannot be said that Haynes et al. (1996) provide evidence that the instant invention was enabled as of the effective filing date which is 10/22/93, for the foregoing reasons.

Haynes et al. (1996) further confirms the unpredictability for DNA vaccination in large mammals. The authors note the studies of Wolff and coworkers which demonstrated that direct muscle inoculation of plasmid DNA resulted in low level, sustained gene expression in rodent muscle. However, gene expression following muscle inoculation in nonhuman primate muscle was demonstrated at a significantly reduced efficiency (page 38, column 2, paragraph 2). The authors further refer to the advantage of gene gun-based DNA vaccine technology as being particularly useful in "larger animals where the potential for muscle injection is less clear" (page 38, column 2, paragraph 3). The unpredictability in the art of DNA vaccination also extends to the particular route of administration used. In describing the use of particle-mediated DNA immunization to produce protective immune responses in mice, the authors note that "[p]arallel immunizations via the intramuscular, intravenous, intraperitoneal, and intradermal routes, using considerably greater amounts of DNA, did not achieve comparable levels of vaccine protection." Thus, results obtained in mice by gene gun methods are not predictive of results obtained using other routes of administration. The authors go on to report that "[a]dditional data comparing the relative efficacy of muscle injection and particle-mediated DNA immunization of the

epidermis … demonstrated that considerably stronger immune responses could be elicited against several antigens using as little as 16 ng of DNA per immunization. Intramuscular injection of as much as 6000-fold more DNA did not achieve comparable immune responses" (page 39, paragraph bridging columns 1-2). Thus, the results obtained by gene gun methods are not predictive of results obtained by intramuscular administration.

At page 11 of the response, Applicants assert that Ertl et al. (1996) cites the work of the inventors to indicate that DNA vaccination produces "both humoral and cell-mediated immunity" and that certain drugs causing muscle damage "improve the efficacy of genetic vaccines." Applicants further note that Ertl cites the work of the inventors to indicate that, compared with traditional vaccines, genetic vaccines result in a longer lasting immune response. Applicants are reminded that a scope of enablement for the use of genes encoding HBV surface antigens has already been acknowledged, which is entirely consistent with the discussion of Ertl. Ertl does not suggest enablement for other antigens. It is noted that the prior art generally acknowledges the critical role of the particular antigen used in DNA vaccination protocols. In a review of genetic immunization, Ertl et al. (1996, Viral Immunology, 9(1):1-9) emphasize the critical role of the antigen, stating that, "although any antigens can be delivered by genetic immunization, some proteins upon expression by plasmid vectors remain immunologically silent. The principles that govern success versus failure of genetic immunization with regard to each individual protein remain to be elucidated" (page 2, paragraph 3). This clearly indicates unpredictability in the art.

Conclusion

No claims are allowable.

This application contains claims 48-53 drawn to an invention nonelected without traverse in the reply filed on July 27, 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history

information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on (571) 272-4517. The central official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

/Anne-Marie Falk/
Primary Examiner, Art Unit 1632